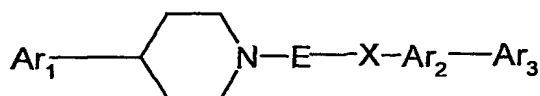


Claims

1 A compound of formula (I)



(I)

wherein

Ar₁ is:

- (i) phenyl, naphthyl or phenyl fused by a C₃₋₈cycloalkyl; or
 - (ii) heterocyclyl selected from the list consisting of: monocyclic radicals and fused polycyclic radicals, wherein said radicals contain a total of from 5-14 ring atoms, wherein said radicals contain a total of from 1-4 ring heteroatoms independently selected from oxygen, nitrogen and sulfur, and wherein individual rings of said radicals may be independently saturated, partially unsaturated or aromatic, provided that at least one ring is aromatic;
- where Ar₁ is independently substituted by at least one R¹ group and is independently substituted by 0-3 R³ groups;

Ar₂ is a phenyl group, a 5-6 membered heteroaromatic group or a bicyclic heteroaromatic group, each of which are optionally substituted by 1-4 groups independently selected from the list: C₁₋₄alkyl, halogen, hydroxy, C₁₋₄alkoxy, C₁₋₆acyl, C₁₋₆acyloxy, amino, C₁₋₄alkylamino, di-C₁₋₄alkylamino, -(CH₂)_nOH, -(CH₂)_nNR_xR_y, -O(CH₂)_nO(CH₂)_mOR², -O(CH₂)_nC(O)NR_xR_y, -O(CH₂)_nCN, C₂alkenyl, -O(CH₂)_nCO₂R², -OSO₂(CH₂)_pCH₃, -OSO₂NR_xR_y and -CO₂(CH₂)_pCH₃;

Ar₃ is:

- (i) phenyl, naphthyl or phenyl fused by a C₃₋₈cycloalkyl; or
- (ii) heterocyclyl selected from the group consisting of monocyclic radicals and fused polycyclic radicals, wherein said radicals contain a total of from 5-14 ring atoms, wherein said radicals contain a total of from 1-4 ring heteroatoms independently selected from oxygen, nitrogen and sulfur, and wherein individual rings of said radicals may be independently saturated, partially unsaturated, or aromatic, providing that at least one ring is aromatic;

wherein Ar₃ is optionally substituted by 1-4 groups independently selected from the group consisting of: hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, C₂₋₄alkenyl, C₂₋₄alkenyloxy, C₁₋₄perfluoroalkoxy, C₁₋₄alkylsulfonylamino (such as -NHSO₂CH₃, -NHSO₂CH(CH₃)₂), fluoroC₁₋₄alkylsulfonylamino (such as -NHSO₂CH₂CF₃), C₁₋₄alkylcarbonylamino, fluoroC₁₋₄alkylcarbonylamino, halogen (such as chlorine), nitrile, nitro, C₁₋₄perfluoroalkyl, C₁₋₄alkylcarbonyl, fluoroC₁₋₄alkylcarbonyl, C₁₋₄alkoxycarbonyl, aminocarbonyl, C₁₋₄alkylaminocarbonyl, di-C₁₋₄alkylaminocarbonyl, C₁₋₄alkylsulfonyl, C₁₋₄alkylaminosulfonyl, di-C₁₋₄alkylaminosulfonyl, C₁₋₄alkylsulfonyl and C₁₋₄alkylsulfoxy;

E is -C₁₋₆alkylene-;

X is -CONR²- or -NR²CO-;

wherein

R¹ is O(CH₂)_nOR²;

R² is C₁₋₄alkyl or hydrogen;

R³ is halogen, C₁₋₄alkoxy or C₁₋₄alkyl;

R_x and R_y are independently C₁₋₄alkyl or hydrogen;

n and m are independently 1-4; and

p is 0-4;

or a physiologically acceptable prodrug, salt or solvate thereof.

2 A compound according to claim 1 wherein Ar₁ is phenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, indolyl, benzofuranyl, benzothiophenyl or indazolyl.

25 3 A compound according to any preceding claim wherein E is n-butylene.

4 A compound according to any preceding claim wherein X is -NR²CO-.

5 A compound according to any preceding claim wherein Ar₂ is phenyl or a 5-6-
30 membered heteroaromatic group.

6 A compound according to claim 5 wherein Ar₂ is optionally substituted by C₁₋₄alkyl, halogen, hydroxy, hydroxyC₁₋₄alkyl or C₁₋₄alkoxy.

35 7 A compound according to any preceding claim wherein Ar₃ is phenyl, pyridyl or thienyl.

8 A compound according to claim 7 wherein Ar₃ is substituted by halogen (e.g. chloro), C₁₋₄perfluoroalkyl (e.g. trifluoromethyl), nitrile, C₁₋₄acyl (e.g. acetyl), C₁₋₄alkylsulfonyl (e.g. methylsulfonyl) or C₁₋₄alkylsulfonylamino.

5 9 A compound according to any preceding claim wherein R¹ is -OCH₂CH₂OR².

10 A compound according to claim 1 wherein

10 Ar₁ is phenyl, naphthyl, 1,2,3,4-tetrahydronaphthyl, indolyl, benzofuranyl, benzothiophenyl or indazolyl; where Ar₁ is independently substituted by at least one R¹ group and is independently substituted by 0-3 R³ groups;

15 Ar₂ is phenyl, pyridyl, thiazolyl, oxazolyl or imidazolyl, each of which are optionally substituted by 1-4 groups independently selected from the list; C₁₋₄alkyl, halogen, hydroxy, hydroxyC₁₋₄alkyl and C₁₋₄alkoxy;

20 Ar₃ is phenyl, pyridyl or thienyl, wherein Ar₃ is optionally substituted by 1-4 groups independently selected from the group consisting of: halogen (e.g. chloro), C₁₋₄perfluoroalkyl (e.g. trifluoromethyl), nitrile, C₁₋₄acyl (e.g. acetyl), C₁₋₄alkylsulfonyl (e.g. methylsulfonyl) and C₁₋₄alkylsulfonylamino;

E is n-butylene;

X is -NR²CO-;

wherein

R¹ is -OCH₂CH₂OR²;

25 R² is C₁₋₄alkyl or hydrogen;

R³ is halogen, C₁₋₄alkoxy or C₁₋₄alkyl; and

n is 1-4.

11 A compound according to claim 1 selected from the list:

30 4-Hydroxymethyl-2-(4-trifluoromethyl-phenyl)-thiazole-5-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide (Example 3);

35 4'-Cyano-biphenyl-4-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide hydrochloride (Example 5);

2-(4-Cyano-phenyl)-4-methyl-thiazole-5-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide, hydrochloride (Example 7);

2-(2,4-dichloro-phenyl)-4-methyl-thiazole-5-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide (Example 8);

2',4'-Chloro-biphenyl-4-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide (Example 9);

4'-Chloro-biphenyl-4-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide (Example 10);
and

4'-Methanesulfonylamino-biphenyl-4-carboxylic acid (4-{4-[1-(2-hydroxy-ethoxy)-5,6,7,8-tetrahydro-naphthalen-2-yl]-piperidin-1-yl}-butyl)-amide (Example 12).

12 A pharmaceutical composition comprising a compound as defined in any preceding claim and a pharmaceutically acceptable carrier or diluent.

13 The use of a compound defined in any one of claims 1 to 11 in the
20 manufacture of a medicament for use in the treatment of conditions resulting from elevated circulating levels of LDL-cholesterol.

14 A compound defined in any one of claims 1 to 11 for use as a medicament